

REMARKS

Claims 36-40, 56-59, and 61-64 have been cancelled (claims 36-40 and 56-59 merely being drawn to non-elected subject matter). Claim 28 has been amended to clarify and further define the present invention. No new matter has been added by virtue of this amendment. Support therefore can be found throughout the specification and in the original claims of the application. In particular, support for the amendment to claim 28 is established, for example, on page 1, line 21 to page 4, line 19, and in the Examples of the present application.

✓ Applicants acknowledge the objections to claim 63 under 37 CFR 1.75. Applicants note that claim 63 has been cancelled, thus rendering the objection moot.

✓ Claim 64 stands rejected under 35 USC §112, second paragraph. Applicants note that claim 64 has been cancelled, thus rendering the rejection moot.

✓ Claims 61 and 63 stand rejected under 35 USC §112, first paragraph. Applicants note that claims 61-63 have been cancelled, thus rendering the rejection moot.

✓ Withdrawal of each of the aforementioned objections and rejections is therefore requested.

The remaining rejections each relate to the prior art and are discussed in combination. Each of the rejections is traversed.

Claims 28, 41-43, 46-47, 50-54, 60, 62 and 64 stand rejected under 35 USC §102(b) over Hammarstrom et al. (EP 0 263 086).

Claims 28, 41-48, 50-51, 54-55, 60, 62 and 64 stand rejected under 35 USC §102(b) over Hammarstrom et al. (EP 0 337 967).

Claims 28, 41-42, 46-51, 54-55, 60, 62 and 64 stand rejected under 35 USC §102(b) over Mellonig et al. (*Int. J. Periodontics Restorative Dent.* 19, 9-19, 1999).

Claims 28-29, 41-55, 60, 62 and 64 stand rejected under 35 USC §102(e) over Gestrelus et al. (2002/0169105 A1).

Claims 28-35, 41-55, and 60-65 stand rejected under 35 USC §103(a) over Gestrelus et al. (2002/0169105 A1).

Claims 28-35, 41-55, and 60-65 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-53 of copending Application No. 09/258,613.

Before addressing the present rejections, a brief summary of Applicant's invention is offered. The present invention is directed, in significant part, to a method for promoting the take of a graft. Applicants' method comprises obtaining a graft from a suitable donor, cell culture and/or tissue, administering to the graft a prophylactically effective amount of an active enamel substance, and placing the pretreated graft on a recipient bed or lesion. Applicants have surprisingly found that use of an active enamel substance in accordance with the invention is particularly beneficial in grafts of non-mineralized tissue, e.g., soft tissue comprising a substantial proportion of epithelial cells, such as skin and mucosa. Methods of the invention promote the taking of the graft, i.e. enhanced attachment of the graft, reduced infection and scarring, and ultimately improved wound healing.

Applicants emphasize that the present invention is directed to the taking of a graft, not merely to the contacting of a tissue with a composition of the application. The within amendments to claim 28 are intended to clarify and further define the steps of Applicants' method

which define the invention.

Referring now to the prior art rejections, Applicants submit that the cited documents do not teach or suggest Applicant's claimed invention in a manner sufficient to sustain a rejection under 35 U.S.C. §102 or §103.

In contrast to the present invention, the two Hammarström et al. references merely disclose effects of enamel matrix substances on the regrowth of new mineralized tissues. Contrary to the position taken in the Office Action, it is respectfully submitted that Example 7 of EP 0263 086 only shows formation of new mineralized tissue brought upon by the application of an active enamel substance. Induction of new tissue formation should not be confused with joining of two pre-existing tissues, e.g., graft and wound bed. Indeed, it is a distinctive feature of the claimed invention that the recipient bed is non-mineralized tissue. (See e.g., amended independent claim 28.)

Mellonig et al. is similarly deficient. For example, that reference explicitly teaches only new formation (neogenesis) of mineralized tissues. In accordance with the disclosure of Mellonig et al., Emdogain (EMD) is only applied onto the mineralized tooth surface. Mellonig et al. expressly define dental reconstruction as reconstruction of mineralized tissues, such as acellular cementum (see, e.g., the discussion in Mellonig et al. which begins on page 17).

Again, it is emphasized that the technical problem to be solved by the present invention, i.e. the taking of a graft, is neither formulated nor anticipated in any of the above-cited documents.

Further, with respect to Gestrelius et al. (2002/0169105 A1), Applicants submit that there is a significant distinction between the healing of a wound and the taking of a graft. Indeed, these are two very distinct processes.

For instance, a method for the taking of a graft is defined through at least two distinct and specific phases, i.e.:

- a) Preventing the initial rejection of the foreign graft tissue. (In accordance with the invention, EMD is employed to modulate the local inflammatory processes, so that the recipient tissue does not reject the graft.)
- b) Facilitating the integration of the graft into the recipient tissue by preventing the ingrowth of epithelial cells into the graft bed. Such ingrowth usually leads to the building of a secondary epithelial layer underneath the graft, which renders it impossible for the graft to attach to the recipient bed. This is especially critical in, for example, burns.

It is only *after* the above functions have been successfully performed that the actual "wound healing" is initiated.

Moreover, normal wound healing is a process that is dependent on induction of *cell and tissue growth*. In contrast, grafting is initially a process that is dependent on *cell and tissue stasis*. In the first 24-48 hours after placing the graft in the recipient bed, EMD is applied primarily to suppress unwanted stimulation of cells of the immune system and unwanted epithelial cell or tissue growth.

Consistent with the foregoing arguments, Applicants also submit that no double-patenting would exist in view of co-pending application USSN 09/258,613. Indeed, the method of the present application is neither disclosed nor even suggested in that reference.

Accordingly, each of these rejections is properly withdrawn.

For example, see *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978) ("[r]ejections under

35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.")

Additionally, it is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references to make the claimed invention, nor would there be a reasonable expectation of success.

In view thereof, reconsideration and withdrawal of the §102 and §103 rejections are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES
(Additions are underlined; deletions are bracketed.)

IN THE CLAIMS

Claims 36-40, 56-59, and 61-64 were cancelled without prejudice or disclaimer.

Claim 28 was amended as follows:

28. A method for promoting the take of a graft in [non-mineralized tissue] a mammal in need thereof, the method comprising: [administering to a mammal in need thereof a prophylactically effective amount of an active enamel substance]

taking the graft from one or more of the group consisting of a suitable donor, a cell culture and a suitable tissue,

administering to said graft a prophylactically effective amount of an active enamel substance, and

placing the graft, pre-treated with the active enamel substance, on a non-mineralized tissue recipient bed or lesion.